Journal of Biomechanics 46 (2013) 2682–2687

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Gait variability magnitude but not structure is altered in essential tremor

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ARTICLE INFO

Article history:
Accepted 31 July 2013

Keywords:
Gait
Variability
Essential tremor
Motor control
Cerebellum

ABSTRACT

Essential tremor (ET) is a common tremor disorder affecting postural/action tremor of the upper extremities and midline. Recent research revealed a cerebellar-like deficit during tandem gait in persons with ET, though spatiotemporal variability during normal gait in ET has been relatively ignored. The first purpose of this study was to investigate gait variability magnitude and structure in ET as compared to healthy older adults (HOA). To address this issue, 11 ET and 11 age-matched HOAs walked on a treadmill for 5 min at preferred walking speeds. HOAs walked for an additional minute while speed-matched to an ET participant. The second purpose was to describe the clinical correlates of gait variability in this population. To address this aim, 31 persons with ET walked on a treadmill for 5 min and completed the Fahn–Tolosa–Marin Tremor Rating Scale. Gait variability magnitude was derived by calculating coefficients of variation in stride length, stride time, step length, step time, and step width. Gait variability structure was derived using a detrended fluctuation analysis technique. At preferred walking speeds, ET participants walked significantly slower with significantly increased variability magnitude in all five spatiotemporal gait parameters. At speed-matched walking, ET participants exhibited significantly higher step width variability. Gait variability structure was not different between groups. We also observed that gait variability magnitude was predicted by severity of upper extremity and midline tremors. This study revealed that self-selected gait in ET is characterized by high variability that is associated with tremor severity in the upper extremity and midline.

1. Introduction

Essential tremor (ET) is one of the most prominent movement disorders in the adult population (Louis et al., 1998; Louis and Ferreira, 2010). Persons with ET have a syndrome typically characterized by an upper extremity action tremor which, in many patients, leads to increased difficulty in performing activities of daily living and a reduced quality of life (Chandran and Pal, 2013). As such, significant effort has been put into developing our understanding of upper extremity tremor and its implications on motor control in ET (Louis, 2005). Hence, motor control deficits in this population have been classically described as dysfunctional control of the upper extremities, trunk, head, and neck.

More recent findings have expanded upon the traditional understanding of motor control in persons with ET and have suggested that lower extremity function is also abnormal in ET. Midline tremors experienced by persons with ET may disrupt control of axial movements involved with locomotor and postural control. Several studies have described deficits during normal and tandem gait in persons with ET (Kronenbuerger et al., 2009; Louis et al., 2010; Rao et al., 2011; Stolze et al., 2001). Rao et al. (2011) documented that persons with ET spent an increased percentage of the gait cycle in double limb support, exhibited greater step time asymmetry, and walked with a reduced cadence and slower velocity when compared to age-matched controls. Conversely, other studies have observed only subtle differences in traditional gait performance, but have revealed marked cerebellar-like dynamic balance disturbance during tandem walking (Hoskovcová et al., 2013; Louis et al., 2010; Stolze et al., 2001). Louis et al. (2010, 2012) have recently elaborated on the clinical correlates of these findings, demonstrating associations between severity of midline tremors and worsened performance on gait and balance tests. Parisi

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http://dx.doi.org/10.1016/j.jbiomech.2013.07.039

et al. (2006) also noted worsening of functional mobility in persons with ET who experienced head tremor as compared to those without head tremor. Though it has been postulated that these associations between midline tremor and worsening of gait may be indicative of the presence of a midline cerebellar syndrome in ET (Louis et al., 2010), more work is needed to characterize disturbances in gait variability.

Classical spatiotemporal gait characteristics such as gait velocity and step length provide important information pertaining to global gait performance; however, these parameters suggest very little about the variability of gait patterns. To date, only a few studies have examined gait variability in persons with ET (Fasano et al., 2010; Rao et al., 2011; Stolze et al., 2001). This is surprising considering the well-known associations between increased gait variability, dynamic instability, and fall risk (Brach et al., 2005; Callisaya et al., 2011; Toebes et al., 2012). These studies have reported inconclusive results, perhaps due to the analysis of a relatively limited number of strides and the reliance upon clinical measures such as ataxia ratio. An ataxia ratio may be clinically-relevant, but confounds directional variability analyses by combining deviations in step length, step width, and step height into a singular measure (Stolze et al., 2001). Previous research on gait variability in ET has also been limited exclusively to linear measures of the magnitude of variability. Nonlinear measures have often supplemented these linear analyses by describing the structure of variability in gait in other populations (Hausdorff et al., 1997; Kaipust et al., 2012; Wuehr et al., 2013), including persons with cerebellar disease (Wuehr et al., 2013). Previous research by Hausdorff et al. (1995) has suggested that the spinal central pattern generators (CPGs) theorized to govern the regulation of steady-state gait possess a certain type of "memory" which regulates gait variability. This work suggests the presence of long-range correlations between gait cycles over time (Hausdorff et al., 1995). However, in elderly and some pathological populations, this CPG "memory" deteriorates and gait variability patterns become less-correlated and sometimes more random (Hausdorff et al., 1997), perhaps indicating disruption of CPG control of locomotion. Given the difficulty frequently observed in ET during tandem gait (Louis et al., 2012; Rao et al., 2011; Stolze et al., 2001), research into the magnitude and structure of gait variability patterns may provide further insight into ET locomotor control deficits.

The goals of this study were two-fold. First, we aimed to compare both the magnitude and the structure of gait variability in persons with ET to neurologically-healthy older adults (HOA). Second, we investigated individual items on the Fahn–Tolosa–Marin Tremor Rating Scale (TRS) (Stacy et al., 2007) as predictors of gait variability parameters to examine potential relationships between gait variability and clinical measures of ET disease severity. Consistent with previous research on classic cerebellar disorders, we hypothesized that persons with ET would demonstrate increased step length, step width, and step time variability when compared to HOA (Serrao et al., 2012) while the structure of the variability would be similar between groups when walking at preferred speeds (Wuehr et al., 2013). Based on previous research suggesting a link between gait difficulty and midline tremor severity (Hoskovcová et al., 2013; Louis et al., 2010, 2012; Parisi et al., 2006), we also postulated that measures of gait variability magnitude would be predicted by the severity of midline tremors.

2. Methods

2.1. Participants

Thirty-one participants with ET (mean ± SD age: 66.5 ± 9.6 yr, mean height: 175.6 ± 11.6 cm, mean body mass: 94.2 ± 23.4 kg, mean TRS motor (items 1–14) score: 32 ± 14, mean TRS ADL (items 15–21) score: 10 ± 7, mean TRS total score: 43 ± 19) were referred from the Center for Movement Disorders and Neurorestoration at the University of Florida and participated in this study. Thirteen ET participants were taking either a beta-adrenergic antagonist, an anticonvulsant, or both while the remaining 18 ET participants were not taking any medication specifically intended to reduce tremor. For the cross-sectional portion of the study, 11 healthy older adults (HOA; mean age: 63.6 ± 7.8 yr, mean height: 170.9 ± 7.2 cm, mean body mass: 75.7 ± 13.3 kg) participated and were age-matched within 1 yr of the persons with ET. Independent samples *t*-tests did not reveal any differences in mean age, height, or body mass between groups (all $p > 0.05$). All ET participants had been previously evaluated and diagnosed by a movement disorder neurologist. Six ET participants in the cross-sectional portion of the study were medicated while the remaining five ET participants were not. None of the participants had undergone deep brain stimulation implantation and all participants were unaffected by musculoskeletal and neurological impairment (with the exception of ET). HOA were enrolled from the university and neighboring community. Before participation in the study, all participants provided written informed consent that was approved by the University's Institutional Review Board. The participants with ET also completed the TRS prior to performing the gait trials.

2.2. Fahn–Tolosa–Marin Tremor Rating Scale (TRS)

The TRS is composed of 21 individual items (many with sub-scores for assessment of resting, postural, and action/intention tremor) scored on a scale from 0 (normal) to 4 (most severe) such that the minimum score is zero and the maximum score is 144. The motor section (items 1–14) includes assessment of tremor at specific anatomical locations (face, tongue, voice, head, right and left upper extremity, trunk, right and left lower extremity) as well as during specific upper extremity motor tasks (handwriting, spiral drawing, pouring). The ADL section (items 15–21) includes assessment of tremor and its patient-reported interference with specific activities of daily living (speaking, feeding, bringing liquids to mouth, hygiene, dressing, writing, and working). Scores in each section are summed to motor and ADL scores. The total TRS score is the sum of the motor and ADL scores (or the sum of all TRS items). The TRS was scored by a movement disorders neurologist. For further details on the TRS, please see Stacy et al. (2007).

2.3. Treadmill gait analysis

All participants were fitted with 35 passive retroreflective markers placed in accordance with the Vicon Plug-in-Gait full body marker set. The participant's preferred walking speed was determined by gradually speeding up the treadmill from a stop until the participant identified that the treadmill speed was similar to the pace at which they felt would typically walk down the sidewalk or down a hallway. Participants then walked on a treadmill for 5 min at their self-selected preferred walking speeds (mean number of strides: ET 235 ± 33.2, HOA 257 ± 24.3). After a short rest, HOA performed an additional minute of treadmill walking at a speed matched to a corresponding age-matched ET participant in order to examine any effect of walking speed on gait variability between the groups. The participants with ET did not walk at speeds matched to the HOA as many of the ET participants could not comfortably walk at these faster speeds. Kinematic data were collected throughout the duration of the 5-min treadmill walking trial using a 10-camera motion capture system (120 Hz; Vicon Nexus, Vicon, Oxford, UK). Heel-strikes and toe-offs were manually labeled based on marker trajectory profiles.

Modified stride length was calculated for the treadmill as the distance traveled by the ankle marker along the antero-posterior walking axis from heel-strike to toe-off (Reisman et al., 2005). Stride time was calculated as the time between two consecutive heel-strikes of the same limb. Step length was calculated as the distance between the ankle markers along the antero-posterior walking axis at heel-strike. Step time was calculated as the time between contralateral heel-strikes. Step width was calculated as the distance between the ankle markers along the medio-lateral axis at heel-strike. Mean and coefficient of variation (CV = standard deviation/mean × 100%) were calculated over all strides across the entire 5-min treadmill walking trial for all five spatiotemporal gait parameters.

2.4. Detrended fluctuation analysis

We then applied a detrended fluctuation analysis (DFA) technique to analyze the structure of the variability across all strides within the 5-min treadmill trial. DFA techniques have been previously applied to physiological signals (Peng et al., 1993) including stride-to-stride gait variability (Hausdorff et al., 1995). First, the spatiotemporal gait data is listed as a time-series. These time-series signals are then integrated and partitioned into data boxes with length ranging from 4 data points per box to $N/4$ points per box, where N is the total number of spatiotemporal gait data points collected over the 5-min treadmill trial. A linear least-squares line is fit to the data within each box of 4 to $N/4$ points and the average fluctuation of the physiological gait data around the least-squares line is calculated for each individual data box. The logs of the average fluctuation values for all data boxes are then plotted against the logs of the individual data box sizes. The ultimate output of the DFA is the slope of the linear least-squares line fit to this log–log plot,